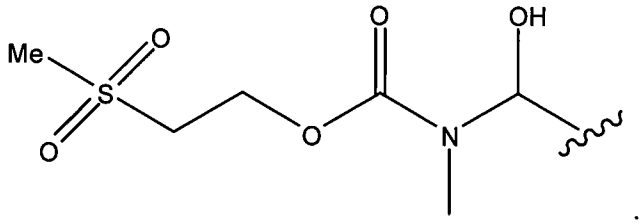


Remarks

Claims 1, 4-6, 8 and 10-12 are pending after entry of the foregoing amendment. Claim 1 is amended herein. Support for the amendments may be found at least at the following pages: page 7, line 11 to page 8, line 17 (definition of C_{3-20} heterocyclyl), page 8, line 19 to page 10, line 12 (definition of C_{5-20} aryl), page 10, lines 23-27 (definition of ether substituent), and page 27, line 21 to page 28, line 5 (N_{10}-C_{11} imine bond prodrugs). In addition, the structure in claim 1 was amended to indicate N_{10} and C_{11}. No new matter is added by these amendments.

Claims 11 and 12 are newly added. Support for the new claims may be found at least at page 27, line 21 to page 28, line 5.

Rejections Under 35 U.S.C. § 112

Claims 1-6, 8 and 10 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the invention. Claim 1 was rejected as not being in proper Markush form. Applicants have amended claim 1 to correct this error and request that the rejection be withdrawn.

Additionally, the claims were rejected for the use of the term "prodrug" because the nature of the claimed prodrugs is not known. Applicants have amended claim 1 to indicate that the prodrugs are N_{10}-C_{11} imine bond prodrugs. These prodrugs contain a nitrogen protecting group which can be removed *in vivo* bound to the nitrogen of the imine group. The carbon of the imine group bears a hydroxyl, ester or thioester group. Examples of such prodrugs are described at page 27, line 21 to page 29, line 5 of the present specification. Additional examples are found in WO 00/12507 which is incorporated by reference in the present specification. Applicants respectfully submit that this amendment obviates the rejection and request that it be withdrawn.

The claims were rejected for the use of the term "substituted" without specifying the substituents. Applicants respectfully submit that this rejection was addressed in the previous response and that the claims do not contain the term "substituted" without specifying the substituents. Applicants respectfully request that the rejection be withdrawn. If the examiner disagrees, Applicants respectfully request additional information regarding the use of the term "substituted" so that Applicants can address the rejection.

The claims were also rejected for the use of the terms "C_{3-20} heterocyclyl" and "C_{5-20} aryl." Applicants have deleted these terms from the claims and replaced them with additional description of the groups from the specification and therefore respectfully request that the rejection be withdrawn. Applicants have also deleted the term "ether" and replaced it with additional description of the term from the specification.

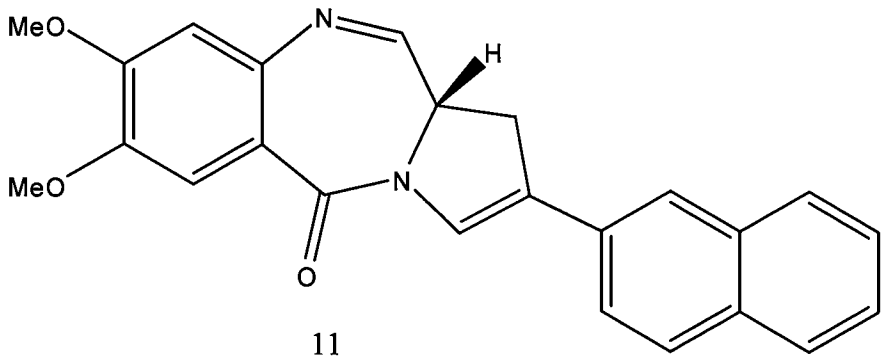
Rejections Under 35 U.S.C. § 103

Claims 1-6, 8 and 10 were rejected under 35 U.S.C. § 103(a) as unpatentable over Thurston et al. (WO 00/12508). The Office Action asserts that Thurston et al. teaches a generic group of compounds that embraces Applicants' claimed compound and acknowledges that the claimed compounds differ from those in the prior art by limiting R^2 to optionally substituted naphthyl, thiophenyl, furanyl and substituted phenyl. The Office Action asserts that the closest prior art compound is that where R^2 is methoxy substituted phenyl or phenyl. Thus, it is the position of the USPTO that the claimed invention is obvious. Further, it is the USPTO's position that one of ordinary skill in the art would have been motivated to select the claimed compounds from the genus because the compounds were suggested by the reference as a whole and would have had the expectation that any of the species of the prior art genus would have had similar properties.

Applicants respectfully disagree that one of ordinary skill in the art would have been led to the claimed compounds by the disclosure of the prior art genus. However, in the interests of advancing prosecution, Applicants have limited R_2 to optionally substituted naphthyl. Applicants respectfully submit that one of ordinary skill in the art would not have been motivated to select the naphthyl-containing compounds from the genus of Thurston et al. Thurston et al. teaches that the most preferred compounds are those where R_2 is lower alkyl having 1 to 10 carbon atoms. Aryl groups are listed as preferred, but the only examples given are phenyl and

substituted phenyl. There is no disclosure of fused ring aryl groups at all, let alone naphthyl groups.

An exemplary compound of the claimed invention is compound 11 shown below:



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In the specification, Applicants presented comparative testing that showed that the claimed compounds are significantly better than the prior art compounds. The compounds of the present invention were tested in a clonogenic assay described at pages 61-62 of the specification. The IC_{50} values of the compounds were determined by plotting compound concentration versus cell viability. The prior art compound C1 had an IC_{50} value of 19.33 against a breast cancer cell line. In stark contrast, a compound according to the present invention 11 had an IC_{50} of 0.22. (Specification at 63).

In addition to the data presented in the specification at pages 61-64, Applicants have now completed additional comparative testing between the claimed compounds and the prior art compounds. The results are described in the accompanying declaration of Dr. Philip Howard.

Specifically, the claimed compounds show significantly better activity against a range of cancer cell lines as compared to the prior art compounds. For example, a compound according the present invention had an IC_{50} of 1.32 against a renal cancer cell line as compared to 20.50 for the prior art compound; and IC_{50} of 6.50 as compared to 44.50 against a lung cancer cell line; and 1.80 as compared to 40.00 against a melanoma cell line. (Declaration of Philip Howard at ¶ 8). Thus, the claimed compounds are substantially more active than the compounds of the prior art. (Id. at ¶ 9). Given the data in the accompanying Declaration of Dr. Philip Howard and the arguments presented herein, Applicants respectfully submit that the

currently pending claims are not obvious over the prior art. Applicants, therefore, respectfully request that the rejections be withdrawn.

Obviousness-Type Double Patenting Rejection

Claims 1-6 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 40 of U.S. Patent No. 7,049,311. U.S. Patent No. 7,049,311 is related to Thurston et al. As discussed above with respect to Thurston et al., Applicants respectfully submit that the currently pending claims are indeed patentable over claims 1 and 40 of U.S. Patent No. 7,049,311 and request that the rejection be withdrawn.

CONCLUSION

In view of the remarks presented herein, it is believed that this application is now in condition for allowance. The Examiner is strongly encouraged to contact the undersigned at the phone number below should any issues remain with respect to the application.

Respectfully submitted,

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